His-Leu-Gly-Gly-Ala-Lys-Gln-Ala-Gly-Asp-Val) (SEQ ID NO: 49), leptin (93-105) (Asn-Val-Ile-Gln-Ile-Ser-Asn-Asp-Leu-Glu-Asn-Leu-Arg) (SEQ ID NO: 50), GR 83074 (Boc-Arg-Ala-DTrp-Phe-DPro-Pro-Nle-NH_2) (SEQ ID NO: 51) Tyr-W-MIF-1 (Tyr-Pro-Trp-Gly-NH_2) (SEQ ID NO: 52), parathyroid hormone related peptide (107-111) (Thr-Arg-Ser-Ala-Trp) (SEQ ID NO: 53), angiotensinogen (1-14) Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His-Asn (SEQ ID NO: 54), and Leupeptin (Ac-Leu-Leu-Arg-CHO).

F13 Cancelled

REMARKS

As an initial matter, Applicant requests that the USPTO acknowledge priority to Danish Patent Application No. 0317/98 as filed on March 9, 1998. A certified copy of the Danish priority document was submitted to the Office on May 11, 2001. Acknowledgement of Applicants' foreign priority claim and receipt of the Danish priority document on the Examiner's PTO-326 form would be greatly appreciated.

Claims 9, 19, 54 and 57 have been canceled without prejudice or disclaimer of any subject matter.

Claims 1, 7, 8, 10, 24, 52, 54, 55, 57, 58, 64, 68, 75 and 77 have been amended and new claims 78-81 added. Support for the amendments and new claims can be found throughout the instant application including the Drawings and claims as filed originally.

Claims 1, 52, 54, 57, 64, and 68 have been amended to recite peptide conjugates in which "Z" is more precisely defined. For instance, see claims 1, 52, 54, 57, 64 in which "Z" is a homopolymer in which each amino acid unit therein is Ala, Leu, Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His, Met, Orn or the amino acid unit shown as formula I. See also claim 68 in which "Z" is defined as a specific lysine polymer.

New claims 78, 79, 80 and 81 have been drafted along lines of claims 1, 52, 64, and 68, respectively and as amended, except that the new claims feature "consisting of" language in the preamble.

Claims 11, 12, 24, 25, 68 have been amended to put a colon after the abbreviation for "number" in the sequence identifiers. Claim 77 has been amended to add a sequence identifier number 122.

No new matter has been added by virtue of the claim amendments or new claims.

At pg. 2 of the Office Action, the Examiner requested submission of a substitute specification. The substitute specification will follow this submission under separate cover. Included with the substitute specification will be a revised sequence listing.

Claims 1, 2, 6-12, 19, 20, 24-26, 29-32, 52-61, 63-67, 70, and 73-77 stand rejected under 35 USC §112, first paragraph, as not being enabled by the present specification. At pgs. 2-3. Applicants respectfully traverse particularly in view of the present claim amendments.

On pg. 3 of the Action, the USPTO alleged that Applicants "admitted" in the prior response (submitted Nov. 8, 2002) that minor changes in the structure of the claimed compounds can eliminate activity. Applicants have reviewed the prior response and can find no such admission. What Applicants said in the prior response was that the cited Docherty and Burger references reported substantial variation in the activity of particular homopolymers. In the face of that uncertainty in the references themselves, Applicant took the position that there was no basis for an obviousness rejection. See the prior response at pg. 19.

Respectfully, no credible basis for maintaining the instant rejection under 35 USC §112, first paragraph, has been made. Merely treating Applicants' discussion of what Docherty and Burger reported as an "admission" is not sufficient grounds for rejecting the claims. As formulated, the rejection provides no reasonable explanation about why practice of the invention would require "undue experimentation".

Unlike the Office position, the present specification fully satisfies the "how to make" and "how to use" requirement of 35 USC §112, first paragraph, particularly in view of the present claim amendments. For example, the specification as filed originally provides abundant support for making and using the claimed peptide conjugates.

In view thereof, reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1, 2, 6-12, 19, 20, 24-26, 29-32, 52-61, 63-67, 70, and 73-77 stand rejected under 35 USC §112, first paragraph as containing subject matter that was not described in the specification. Applicants respectfully traverse in part. Claims 9, 19, 54 and 57 have been canceled.

The USPTO took the position that there is no support in the case for recitation of "Z comprises at least two amino acid units". While Applicant must disagree with this position for reasons advanced in the prior response, basis for this rejection has been addressed by this response. In particular, the phrase has been removed from the rejected claims solely to advance prosecution of the case.

The USPTO also took the position that there is no support in the case for recitation of "X is heteropolymeric". Applicant respectfully disagrees.

As mentioned in the prior response , the test for determining if Applicant's specification complies with the written description requirement is that it reasonably conveys to one of skill in the field that he had possession of the claimed subject matter as of the priority date. There is no obligation that the inventor must satisfy the written description requirement by literally describing the claimed subject matter (*in haec verba*). See MPEP §2163.02. Instead, the test is that Applicant's specification must **reasonably convey** the inventive concept embodied in the claims to the worker reading his case.

Applicant's specification fully satisfies the written description requirement as discussed above. Support for "heteropolymeric" can be found on pg. 9, line 15 to pg. 11, line 27 (disclosing a variety of heteropolymeric sequences). See also claim 24 as filed originally.

Moreover, a worker reading the instant specification would readily understand that the Applicant was in possession of a variety of heteropolymeric peptide sequences as of the filing date. In support, Applicant submits herewith a peer-reviewed research article that was published well before the priority date of the instant case. As understood, it references peptide sequences as "heteropolymer sequences". Dinner, A.R. (1996) *PNAS (USA)* 93: 8356-8361 (copy provided with this submission). In particular, see pg. 8356, col. 1 in which a peptide comprising 27 amino acid units (referred to as a "27-mer") is mentioned as a heteropolymer sequence:

> Simulations of **27-mer random heteropolymer sequences** on a cubic lattice showed that a necessary and sufficient condition for satisfying the folding requirements of the model is that the native state is a pronounced global energy minimum with a large energy gap between the ground state and the rest of the states.

Accordingly, a worker would understand that the present specification reasonably conveyed that the inventor had full possession of the claimed subject matter as of the priority date. Heteropolymeric peptide sequences are amply supported and described throughout the instant disclosure.

In view thereof, reconsideration and withdrawal of the rejection are earnestly requested.

Claims 1, 2, 6-12, 19, 20, 24-26, 29-32, 52-61, 63-67, 70, and 73-77 were rejected under various grounds under 35 USC §112, second paragraphs. Although Applicant respectfully disagrees that the claims are indefinite in any way, basis for the rejection has been addressed. The claims have been amended as suggested by the Examiner.

Claims 1 and 52 stand rejected as anticipated by U.S. Pat. Nos. 5,968,513 and 5,723,129 to Gallo and Potter, respectively. At pgs. 6-7 of the Action. The rejections are addressed together in the interest of brevity .

As amended, claims 1 and 52 feature peptide conjugates in which Z is defined as a particular homopolymer. As cited, Gallo and Potter do not disclose any peptides that include such a sequence. Accordingly, claims 1 and 52 are not anticipated and the rejection should be withdrawn.

Claim 68 stands rejected as being anticipated by U.S Pat. No. 5,330,971 to Wells. Although Applicants respectfully disagree with the position taken, basis for it has been addressed by this submission.

The Office alleged that the following IGF-1 sequence disclosed by Wells at col. 1, line 20, anticipates claim 68.

10 20 30 40 50 60 70
GPETLCGAEL VDALQFVCGD RGFYFNKPTG **YGSSSRRAPQ** TGIVDECCFR SCDLRRLEMY CAPLKPAKSA

In formulating the rejection, the Office stated that "X" of claim 68 can be residues 30-41 of the IGF-1 sequence (bold text). Action at pg. 8. The Action does not specify where "Z" of claim 68 can be found in Wells' IGF-1 sequence. However it was pointed out that Wells' Lys residues at positions 65 and 68 (bold) support the rejection. Applicant must respectfully disagree.

For instance, claim 68 has been amended to recite a "Z" sequence that includes a lysine polymer having one of the following structures: Lys_p-Xaa_q or Xaa_p-Lys_q in which Xaa can be Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Arg, His, Orn, 2,4-diaminobutanoic acid, 2,3-diaminor ropanoic acid or Met . See claim 68 as amended. As cited, Wells' peptide does not

have such a sequence. Accordingly, there is no basis for maintaining the rejection and it should be withdrawn.

Applicant notes that according to the USPTO if applicant claimed a compound that included benzene, a reference reporting phenol or toluene would anticipate (Action at pgs. 8-9):

> To take a simple example, suppose that a given applicant were claiming any compound that "comprises" benzene. If a given reference were to disclose phenol or toluene, such a reference would anticipate the claim. Or suppose that an applicant were claiming any compound that comprises phenylalanine. Similar to the foregoing, a reference which discloses the amino acid tyrosine would anticipate such a claim.

Respectfully, that position is at odds with US patent law. It is beyond dispute that for a reference to anticipate under §102 it must **identically disclose** the invention. Thus if Applicant were claiming a compound that included benzene that was otherwise novel, the claim would not be anticipated by a reference disclosing phenol or toluene. Those compounds are chemically distinct from benzene. Accordingly, there would be no basis for making such a rejection.

Claims 1, 2, 6-12, 19, 20, 24-26, 29-32, 52-61, 63-65, 70, and 74-76 stand rejected as being obvious in view of Docherty or Burger. Action at pgs. 11-12. The same claims were also deemed obvious in view of Sumner-Smith. Action at pgs. 12-13. Both rejections are addressed together in the interest of brevity.

Applicant respectfully traverses both obviousness rejections. No *prima facie* case has been made in either case.

According to the USPTO, two rather old decisions (*Shetty* (decided in 1977)) and *Hass & Susie* (decided in 1944)) "carve out an exception to the generalization that providing motivation in a §103 rejection is advisable". Action at pg. 12. Respectfully, that position is at odds with more recent rulings from the Federal Circuit.

Since the old *Shetty* and *Hass & Susie* decisions, the Federal Circuit has repeatedly held that for an obviousness rejection to stand, the Office bears the burden of showing a specific teaching, suggestion or motivation in the cited art to make the claimed invention.

See Brown & Williamson Tobacco Corp. v. Philip Morris Inc., 229 F.3d 1120, 1124-25, 56 USPQ2d 1456, 1459 (Fed.Cir.2000):

> **a showing of a suggestion, teaching, or motivation to combine the prior art references is an essential component of an obviousness holding** (quoting *C.R. Bard, Inc., v. M3 Systems, Inc.*, 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed.Cir.1998));

See *In re Dembiczak,* 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed.Cir.1999):

> **our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references.**

See *In re Dance,* 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed.Cir.1998):

> **there must be some motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant;**

See *In re Fine,* 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed.Cir.1988):

> **teachings of references can be combined *only* if there is some suggestion or incentive to do so.** (quoting *ACS Hosp. Sys., Inc. v. Montefiore Hosp.,* 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed.Cir.1984)

The CAFC decisions are abundantly clear. In the absence of some teaching, suggestion or motivation to make the claimed invention, there is no basis for rejecting the claims under §103. In particular, the Office has not pointed to any motivation to make the claimed invention in view of the art cited. On this basis alone, no *prima facie* case has been made.

Moreover, it is not seen how the decisions cited by the Office (one almost 60 years old) outweigh the much more recent rulings from the Federal Circuit. Clearly, the USPTO bears the burden of showing some **teaching, suggestion or motivation** in the cited references or

elsewhere to make the invention. That burden has simply not been met in formulating the present rejection.

Accordingly, no *prima facie* case exists and the instant rejection should be withdrawn.

Applicant respectfully disagrees with the rejection on further grounds.

The Office position is grounded in the belief that it would be obvious to add or subtract a single methylene group on an amino acid side chain of polylysine (Docherty or Burger) and polyarginine (Summer-Smith). Action at pgs11-12. Specifically, the Office alleged that it would be obvious to modify polylysine by changing a single lysine residue to Orn or APG. No specific teaching, suggestion or motivation to make that molecule has been made of record. Rather than apply the correct standard for determining obviousness as set forth by the CAFC as it should, the Office offered at pg. 12 of the Action that:

> The peptide chemist of ordinary skill would recognize the benignity of the change in question, the cited cases (*Shetty* and *Hass & Susie*) carve out an exception to the generalization that providing motivation in a §103 rejection is advisable.

Respectfully, that position is without merit.

As noted in the prior response, the cited references reported substantial changes in the biological activity of polyarginine, polyhistidine, and polylysine when small changes were made. For instance, activity changes were reported to be influenced by length of the homopolymer, pH, charge positioning and other factors. See the prior response, and Figures 2, 3 and pg. 1564, cols. 1-2 of Docherty; and Burger at pg. 19 and 20-21, for instance.

In the face of this uncertainty, it is not seen how the Office can allege that a peptide chemist would recognize the "benignity" of changing a lysine residue of polylysine to Orn or APG. The cited references do not teach, suggest or provide any motivation to make that change.

For example, both Docherty and Burger report substantial variation in the activity of polyarginine, polyhistidine and polylysine homopolymers. Within each type of homopolymer, the references disclose further activity variation. Given the "dual" activity variation reported between different homopolymers and within the same type of homopolymer, there is no basis for asserting that a worker in the field would treat small changes to the homopolymers as "benign".

At best, the USPTO assertion that a peptide chemist would recognize the "benignity" of changing a single amino of polylysine to Orn or APG is conclusory. It is certainly not supported by the art of record in this case which as cited, does not suggest, teach or provide any motivation to make such a change. The Federal Circuit has cautioned against using unsupported general knowledge and conclusory statements to negate patentability under §103:

> In an **obviousness determination**, the factual question of motivation to combine prior art is material to patentability, and **cannot be resolved on subjective belief and unknown authority**.
>
> * * * *
>
> the examiner and the Board of Patent Appeals and Interferences are presumed to act from the viewpoint of a person having ordinary skill in the art to which the subject matter pertains; thus, when they rely on what they assert to be **general knowledge to negate patentability, that knowledge must be articulated and placed on the record** and the failure to do so is not consistent with either effective administrative procedure or effective judicial review.
>
> * * * *
>
> the Board of Patent Appeals and Interferences **cannot rely on conclusory statements** when dealing with particular combinations of prior art and specific claims, but must set forth the rationale on which it relies.

See *In re Sang-Su Lee* 277 F.3d. 1338, 61 U.S.P.Q2d 1430 (Fed. Cir. 2002)

The USPTO has not articulated and placed on the record how the skilled peptide chemist would know that changing polylysine as suggested would be "benign". The art of record in this case indicates otherwise. Accordingly, no case for obviousness has been made. *In re Sang-Su Lee*, ibid.

Moreover, the position that the peptide chemist would recognize the "benignity" of the change is mere conclusion. It is certainly not supported by the art of record. The Office cannot rely on a conclusory statement to support its obviousness determination. *In re Sang-Su Lee*, ibid.

In view thereof, reconsideration and withdrawal of the obviousness rejections in view of Docherty or Burger, and the Sumner-Smith are respectfully requested.

Claims 1, 24, 52 and 54 stand rejected as being unpatentable over Duguay (JBC: 270: 17566, 1995) and US Pat. No. 5,330,971 to Wells. While Applicant respectfully disagrees with the rejection, grounds for it have been addressed by this submission.

In particular, claim 1 has been amended so that "Z" is a homopolymer comprising Ala, Leu, Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His, Met, Orn, or amino acid units according to formula I. As cited, none of Duguay's C-terminal peptides are such a homopolymer. Accordingly, the cited combination of references is not the claimed invention.

Applicant has reviewed Figure 1 of the Duguay reference but cannot find mention of the peptides cited at pg. 13 of the Action. As understood, Figure 1 of Duguay reports the IGF-1 prohormone processing site in which a single 16 amino acid peptide is disclosed. The smaller peptides cited by the Office are not disclosed per se in Figure 1.

If it is the position of the Office that Duguay discloses the cited peptides, then it is obliged to point to a specific teaching, suggestion or motivation that would lead a worker to select those particular peptides from the larger 16 amino acid peptide sequence disclosed by Duguay in Figure 1. Otherwise, the USPTO is engaging in hindsight reconstruction of Applicant's invention which has been expressly forbidden by the federal courts.

In view thereof, reconsideration and withdrawal of the rejection are requested.

Claims 1, 9, 19, 52, 54, 57, 64, and 68 stand rejected as being obvious under 35 USC §103 as being obvious over U.S. Pat. No. 5,376,530 to De The ("'530") in view of U.S. Pat. No. 6,126,939 to Eisenbach-Schwartz ("'939"). While Applicant respectfully disagrees with the rejection, grounds for it have been addressed. For instance, claims 9 and 19 have been canceled.

Applicant disagrees with the rejection on several grounds.

Claims 1, 52, 54, 57, and 64 have been amended so that "Z" is homopolymeric. As cited, the peptide disclosed by the De The patent (N-K-K-K-K) is not a homopolymer. Accordingly, the cited combination of references is not the invention.

Further, Claim 68 recites particular "X" sequences. See claim 1. The dipeptide Asp-Arg and the cited V-R-N-D-R sequence are not "X" as that variable is currently defined in the claim. Thus, the cited combination of references is not the invention of claim 68.

The '530 patent discloses the V-R-N-D-R-N-K-K-K-K sequence only as part of a substantially larger protein sequence. The USPTO has provided no evidence of a specific teaching, suggestion or motivation that would lead a worker to select that sequence from the much larger peptide disclosed by De The. Respectfully, the rejection is based on impermissible hindsight reconstruction of the invention which is forbidden by the case law.

Moreover, the Office assumes without pointing to any particular teaching or suggestion in the cited references or elsewhere that because the '939 patent reports that Asp-Arg is pharmacologically active, that V-R-N-D-R sequence will be as well. No case for any relationship between the peptides (other than sharing some amino acid residues) has been made of record.

In view thereof, reconsideration and withdrawal of the obviousness rejection are respectfully requested.

The Commissioner is authorized to charge deposit account no. **04-1105** for any fee deemed necessary to consider this submission including the fee for considering new claims 142-145.

Early consideration and allowance of the application are earnestly solicited.

Attached to this submission is a marked-up version of the changes made to the specification and claims. The attached page is captioned "version with markings to show changes made".

Respectfully submitted,

Date: 30 JUNE 03

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 9, 19, 54 and 57 have been canceled without prejudice.

Claims 1, 7, 8, 10, 11, 12, 24, 25, 52, 55, 58, 64, 68, 75 and 77 have been amended as follows.

1. (Amended) A peptide conjugate comprising X and Z,

wherein X is a pharmacologically active heteropolymeric peptide sequence, and

wherein Z is a stabilising peptide sequence[,] of 4-20 amino acid units covalently bonded by its N terminus to the C terminus end of X wherein each amino acid unit in said stabilising peptide sequence Z is [selected from the group consisting of] Ala, Leu, Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His, Met, Orn, [and] or amino acid units of the general formula I

$$-NH-C(R^1)(R^2)-C(=O)- \qquad (I)$$

wherein R^1 and R^2 are selected from the group consisting of hydrogen, C_{1-6}-alkyl, phenyl, and phenyl-methyl, wherein C_{1-6}-alkyl is optionally substituted with from one to three substituents selected from halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, and phenyl and phenyl-methyl is optionally substituted with from one to three substituents selected from C_{1-6}-alkyl, C_{2-6}-alkenyl, halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, or R^1 and R^2 together with the carbon atom to which they are bound form a cyclopentyl, cyclohexyl, or cycloheptyl ring; and

wherein the ratio between the half-life of said peptide conjugate and the half-life of the corresponding pharmacologically active peptide sequence, X, when treated with

carboxypeptidase A or leucine aminopeptidase in about 50 mM phosphate buffer solution at about pH 7.4 at about 37°C or in serum or plasma is at least 2; or a salt thereof], wherein Z comprises at least two identical amino acid units].

7. (Amended) A peptide conjugate according to claim 1, wherein each amino acid unit in Z is [independently selected from the group consisting of] Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His, Orn, 2,4-diaminobutanoic acid, 2,3-diaminopropanoic acid [and] or Met.

8. (Amended) A peptide conjugate according to claim 7, wherein each amino acid unit in Z is [selected from the group consisting of] Glu, Lys [and] or Met.

10.(Amended) A peptide conjugate according to claim [9] 1, wherein Z is $(Lys)_n$, wherein n is an integer in the range from about 4 to about 15.

11. (Amended) A peptide conjugate according to claim 9, wherein Z is Lys4 [SEQ ID NO.] (SEQ ID NO: 55), Lys5 [SEQ ID NO.] (SEQ ID NO: 56) or Lys6 {SEQ NO.] (SEQ ID NO: 62).

12. (Amended) A peptide conjugate according to claim 11, wherein Z is Lys_6 [SEQ ID NO.] (SEQ ID NO: 62).

24. (Amended) The peptide conjugate according to claim 1 or 10, wherein X is selected from the group consisting of enkephalin, Leu-enkephalin, Met-enkephalin, angioten-sin I, angioten-sin II, vasopressin, endothelin, vasoactive intestinal peptide, neurotensin, endorphins, insulin, gramicidin, para-celsin, delta-sleep inducing peptide, gonadotropin-Releasing hormone, human parathyroid hormone (1-34), EMP-1, Atrial natriuretic peptide (ANP, ANF), human brain natriuretic peptide (hBNP), cecropin, kinetensin, neurophysins, elafin, guamerin, atriopeptin I, atriopeptin II, atriopeptin III, deltorphin I, deltorphin II, vasotocin, bradykinin, dynorphin, dynorphin A, dynorphin B, growth hormone release factor, growth hormone, growth hormone releasing peptide, oxytocin, calcitonin, calcitonin gene-related peptide, calcitonin gene-related peptide II, growth hormone releasing peptide, tachykinin, adrenocorticotropic hormone (ACTH),

brain natriuretic polypeptide, cholecystokinin, corticotropin releasing factor, diazepam binding inhibitor fragment, FMRF-amide, galanin, gastric releasing polypeptide, gastric inhibitory polypeptide, gastrin, gastrin releasing peptide, glucagon, glucagon-like peptide-1, glucagon-like peptide-2, LHRH, melanin concentrating hormone, melanocyte stimulating hormone (MSH), alpha-MSH, morphine modulating peptides, motilin, neurokinin A, neurokinin B, neuromedin B, neuromedin C, neuromedin K, neuromedin N, neuromedin U, neuropeptide K, neuropeptide Y, pituitary adenylate cyclase activating polypeptide (PACAP), pancreatic polypeptide, peptide YY, peptide histidine-methionine amide (PHM), secretin, somatostatin, substance K, thyrotropin-releasing hormone (TRH), kyotorphin, melanostatin (MIF-1), thrombopoeitin analogs, in particular AF 12505 (Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala) [SEQ ID NO.] (SEQ ID NO: 14), insulin-like growth factor I (57-70) (Ala-Leu-Leu-Glu-Thr-Tyr-Cys-Ala-Thr-Pro-Ala-Lys-Ser-Glu) [SEQ ID NO.] (SEQ ID NO: 15), insulin-like growth factor I (30-41) (Gly-Tyr-Gly-Ser-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr) [SEQ ID NO.] (SEQ ID NO: 16), insulin-like growth factor I (24-41)(Tyr-Phe-Asn-Lys-Pro-Thr-Gly-Tyr-Gly-Ser-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr) [SEQ ID NO.] (SEQ ID NO: 17) , insulin-like growth factor II (33-40) (Ser-Arg-Val-Ser-Arg-Arg-Ser-Arg) [SEQ ID NO.] (SEQ ID NO: 18), insulin-like growth factor II (33-40) (Tyr-Ser-Arg-Val-Ser-Arg-Arg-Ser-Arg) [SEQ ID NO.] (SEQ ID NO: 19), insulin-like growth factor II (69-84) (Asp-Val-Ser-Thr-Pro-Pro-Thr-Val-Leu-Pro-Asp-Asn-Phe-Pro- Arg-Tyr) [SEQ ID NO.] (SEQ ID NO: 20), growth hormone (GH)-releasing peptide-6 (GHRP-6) (His-DTrp-Ala-Trp-DPhe-Lys-NH2) [SEQ ID NO.] (SEQ ID NO: 21), beta-Interleukin I (163-171) (Val-Gln-Gly-Glu-Glu-Ser-Asn-Asp-Lys) [SEQ ID NO.] (SEQ ID NO: 22), beta-Interleukin II (44-56) (Ile-Leu-Asn-Gly-Ile-Asn-Asn-Tyr-Lys-Asn-Pro-Lys-Leu) [SEQ ID NO.] (SEQ ID NO: 23), Interleukin II (60-70) (Leu-Thr-Phe-Lys-Phe-Tyr-Met-Pro-Lys-Lys-Ala) [SEQ ID NO.] (SEQ ID NO: 24), exendin-4 (GLP-1 analog) (His-Gly-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH2) [SEQ ID NO.] (SEQ ID NO: 25), exendin-3 (GLP-1 analog) (His-Ser-Asp-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser) [SEQ ID NO.] (SEQ ID NO: 26), epidermal growth factor (20-31) Cys(Acm)-Met-His-Ile-Glu-Ser-Leu-Asp-Ser-Tyr-Thr-Cys(Acm) [SEQ ID NO.] (SEQ ID NO: 27), bivalirudin

(Hirulog) [(D-Phe-Pro-Arg-Pro-(Gly)4-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Glu-Tyr-Leu)] (D-Phe-Pro-Arg-Pro-$(Gly)_4$-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Glu-Tyr-Leu) [SEQ ID NO.] (SEQ ID NO: 28), hirulog-1 D-Phe-Pro-Arg-Pro-(Gly)4-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Tyr-Leu [SEQ ID NO.] (SEQ ID NO: 29), C-type natriuretic peptide (1-53) (CNP) (Asp-Leu-Arg-Val-Asp-Thr-Lys-Ser-Arg-Ala-Ala-Trp-Ala-Arg-Leu-Leu-Gln-Glu-His-Pro-Asn-Ala-Arg-Lys-Tyr-Lys-Gly-Ala-Asn-Lys-Lys-Gly-Leu-Ser-Lys-Gly-Cys-Phe-Gly-Leu-Lys-Leu-Asp-Arg-Ile-Gly-Ser-Met-Ser-Gly-Leu-Gly-Cys; Disulfide bridge: Cys37-Cys53) [SEQ ID NO.] (SEQ ID NO: 30), "Mini ANP" (Met-Cys-His-cyclohexylAla-Gly-Gly-Arg-Met-Asp-Arg-Ile-Ser-Cys-Tyr-Arg, disulfide bridge cys2-cys13) [SEQ ID NO.] (SEQ ID NO: 31), Melanotan-II (also known as MT-II, alpha-MSH4-10-NH2, or Ac-Nle4-Asp5-His6-D-Phe7-Arg8-Trp9-Lys10) [SEQ ID NO.] (SEQ ID NO: 32), thymosin alpha1 (TA1) (Ac-Ser-Asp-Ala-Ala-Val-Asp-Thr-Ser-Ser-Glu-Ile-Thr-Thr-Lys-Asp-Leu-Lys-Glu-Lys-Lys-Glu-Val-Val-Glu-Glu-Ala-Glu-Asn) [SEQ ID NO.] (SEQ ID NO: 33), ornipressin (also known as 8-ornithine-vasopressin, (POR-8), vasopressin), Cys-Phe-Ile-Gln-Asn-Cys-Pro-Orn-Gly-NH2, Disulfide bridge: Cys1-Cys6) [SEQ ID NO.] (SEQ ID NO: 34), octreotide (201-995) (DPhe-Cys-Phe-DTrp-Lys-Thr-Cys-Thr-ol; disulfide bridge: Cys2-Cys7) [SEQ ID NO.] (SEQ ID NO: 35), eptifibatide (INTEGRILIN), calcitonin gene-related peptide (CGRP) (Ala-Cys-Asp-Thr-Ala-Thr-Cys-Val-Thr-His-Arg-Leu-Ala-Gly-Leu-Leu-Ser-Arg-Ser-Gly-Gly-Val-Val-Lys-Asn-Asn-Phe-Val-Pro-Thr-Asn-Val-Gly-Ser-Lys-Ala-Phe-NH_2; Disulfide bridge: Cys2-Cys7) [SEQ ID NO.] (SEQ ID NO: 36), endomorphin-1 Tyr-Pro-Trp-Phe-NH2 [SEQ ID NO.] (SEQ ID NO: 37); endomorphin-2 Tyr-Pro-Phe-Phe-NH_2 [SEQ ID NO.] (SEQ ID NO: 38), nociceptin (also known as Orphanin FQ, Phe-Gly-Gly-Phe-Thr-Gly-Ala-Arg-Lys-Ser-Ala-Arg-Lys-Leu-Ala-Asn-Gln) [SEQ ID NO.] (SEQ ID NO: 39), angiotensinogen (1-13) (Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His) [SEQ ID NO.] (SEQ ID NO: 40), adrenomodullin (1-12) (Tyr-Arg-Gln-Ser-Met-Asn-Asn-Phe-Gln-Gly-Leu-Arg) [SEQ ID NO.] (SEQ ID NO: 41), antiarrhytmic peptide (AAP) (Gly-Pro-Hyp-Gly-Ala-Gly) [SEQ ID NO.] (SEQ ID NO: 42), Antagonist G (Arg-DTrp-(nMe)Phe-DTrp-Leu-Met-NH_2), indolicidin (Ile-Leu-Pro-Trp-Lys-Trp-Pro-Trp-Trp-Pro-Trp-Arg-Arg-NH_2) [SEQ ID NO.] (SEQ ID NO: 43), osteocalcin (37-49) (Gly-Phe-Gln-Glu-Ala-Tyr-Arg-Arg-Phe-Tyr-Gly-Pro-Val) [SEQ ID NO.] (SEQ ID NO: 44), cortistatin 29 (1-13) (Glp)-Glu-Arg-Pro-Pro-Leu-Gln-Gln-Pro-Pro-His-Arg-Asp) [SEQ ID NO.] (SEQ ID NO: 45),

cortistatin 14 Pro-Cys-Lys-Asn-Phe-Phe-Trp-Lys-Thr-Phe-Ser-Ser-Cys-Lys; Disulfide bridge: Cys2-Cys13 [SEQ ID NO.] (SEQ ID NO: 46), PD-145065 (Ac-D-Bhg-Leu-Asp-Ile-Ile-Trp) [SEQ ID NO.] (SEQ ID NO: 47), PD-142893 (Ac-D-Dip-Leu-Asp-Ile-Ile-Trp) [SEQ ID NO.] (SEQ ID NO: 48), fibrinogen binding inhibitor peptide (His-His-Leu-Gly-Gly-Ala-Lys-Gln-Ala-Gly-Asp-Val) [SEQ ID NO.] (SEQ ID NO: 49), leptin (93-105) (Asn-Val-Ile-Gln-Ile-Ser-Asn-Asp-Leu-Glu-Asn-Leu-Arg) [SEQ ID NO.] (SEQ ID NO: 50), GR 83074 (Boc-Arg-Ala-DTrp-Phe-DPro-Pro-Nle-NH_2) [SEQ ID NO.] (SEQ ID NO: 51) Tyr-W-MIF-1 (Tyr-Pro-Trp-Gly-NH_2) [SEQ ID NO.] (SEQ ID NO: 52), parathyroid hormone related peptide (107-111) (Thr-Arg-Ser-Ala-Trp) [SEQ ID NO.] (SEQ ID NO: 53), angiotensinogen (1-14) Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His-Asn [SEQ ID NO.] (SEQ ID NO: 54), Leupeptin (Ac-Leu-Leu-Arg-CHO), sandostatin and any modified analogue thereof.

25. (Amended) A peptide conjugate according to claim 1 wherein the conjugate is

H-Tyr-Ala-Asp-Ala-Ile-Phe-Thr-Asn-Ser-Tyr-Arg-Lys-Val-Leu-Gly-Gln-Leu-Ser-Ala-Arg-Lys-Leu-Leu-Gln-Asp-Ile-Met-Ser Arg-Gln-Gln-Gly-Glu-Ser-Asn-Gln-Glu-Arg-Gly-Ala-Arg-Ala-Arg-Leu-Lys_6-NH_2 (GHRH(1-44)(Human)-Lys_6-NH_2) [SEQ ID NO.] (SEQ ID NO: 88);

H-Tyr-Ala-Asp-Ala-Ile-Phe-Thr-Asn-Ser-Tyr-Arg-Lys-Val-Leu-Gly-Gln-Leu-Ser-Ala-Arg-Lys-Leu-Leu-Gln-Asp-Ile-Met-Ser Arg-Gln-Gln-Gly-Glu-Ser-Asn-Gln-Glu-Arg-Gly-Ala-Arg-Ala-Arg-Leu-Glu_6-NH_2 (GHRH (1-44)(Human)-Glu_6-NH_2) [SEQ ID NO.] (SEQ ID NO: 89);

H- Lys_6-Ser-Val-Ser-Glu-Ile-Gln-Leu-Met-His-Asn-Leu-Gly-Lys-His-Leu-Asn-Ser-Met-Glu-Arg-Val-Glu-Trp-Leu-Arg-Lys-Lys-Leu-Gln-Asp-Val-His-Asn-Phe-OH (Lys_6-PTH(1-34)(Human)-OH) [SEQ ID NO.] (SEQ ID NO: 90);

H-Ser-Val-Ser-Glu-Ile-Gln-Leu-Met-His-Asn-Leu-Gly-Lys-His-Leu-Asn-Ser-Met-Glu-Arg-Val-Glu-Trp-Leu-Arg-Lys-Lys-Leu-Gln-Asp-Val-His-Asn-Phe-Lys_6-OH (PTH(1-34)(Human)-Lys_6-OH) [SEQ ID NO.] (SEQ ID NO: 91);

H-His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-Lys_6-OH (GLP-1-(7-36)(Human)-Lys_6-OH) [SEQ ID NO.] (SEQ ID NO: 92);

H-Gly-Gly-Thr-Tyr-Ser-Cys(Acm)-His-Phe-Gly-Pro-Leu-Thr-Trp-Val-Cys(Acm)-Lys-Pro-Gln-Gly-Gly-Lys_6-OH (EMP-1-Lys_6-OH) [SEQ ID NO.] (SEQ ID NO: 93) ;

H- Lys_6-Gly-Gly-Thr-Tyr-Ser-Cys(Acm)-His-Phe-Gly-Pro-Leu-Thr-Trp-Val-Cys(Acm)-Lys-Pro-Gln-Gly-Gly-OH (Lys_6-EMP-1-OH) [SEQ ID NO.] (SEQ ID NO: 94);

H- Lys_6-Gly-Gly-Thr-Tyr-Ser-Cys(Acm)-His-Phe-Gly-Pro-Leu-Thr-Trp-Val-Cys(Acm)-Lys-Pro-Gln-Gly-Gly- Lys_6-OH (Lys_6-EMP-1- Lys_6-OH) [SEQ ID NO.] (SEQ ID NO: 95);

H-Aib-His-2-D-Nal-D-Phe-Lys-$(Lys)_6$-NH_2 (GHRP-$(Lys)_6$-NH_2) [SEQ ID NO.] (SEQ ID NO: 96);

H-Tyr-Gly-Gly-Phe-Leu-Lys-Lys-Glu-Glu-Glu-Lys--OH (Leu-enkephalin-Lys-Lys-Glu-Glu-Glu-Lys-OH) [SEQ ID NO.] (SEQ ID NO: 97);

H-Tyr-Gly-Gly-Phe-Leu-Lys-Glu-Glu-Glu-Glu-Lys--OH (Leu-enkephalin-Lys-Glu-Glu-Glu-Glu-Lys-OH) [SEQ ID NO.] (SEQ ID NO: 98);

H-Tyr-Gly-Gly-Phe-Leu-Lys-Glu-Glu-Glu-Glu-Lys--OH (Leu-enkephalin-$(Lys\text{-}Glu)_3$ [SEQ ID NO.] (SEQ ID NO: 99);

H-Tyr-Gly-Gly-Phe-Leu-$(Dpr)_6$-OH (Leu-enkephalin-$(Dpr)_6$-OH) [SEQ ID NO.] (SEQ ID NO: 100);

H-Lys_6-Tyr-Gly-Gly-Phe-Leu-OH (H-Lys_6-Leu-enkephalin) [SEQ ID NO.] (SEQ ID NO: 101);

H-Tyr-Gly-Gly-Phe-Leu- Lys_6-OH (H-Leu-enkephalin-Lys_6) [SEQ ID NO.] (SEQ ID NO: 11);

H-Lys_6-Tyr-Gly-Gly-Phe-Leu-Lys_6-OH (H-Lys_6-Leu-enkephalin-Lys_6-OH) [SEQ ID NO.] (SEQ ID NO: 102);

Glu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-$(Lys)_6$-OH (GnRH-Lys_6-OH) [SEQ ID NO.] (SEQ ID NO: 103);

Glu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-$(Lys\text{-}Glu)_3$-OH (GnRH-$(Lys\text{-}Glu)_3$-OH) [SEQ ID NO.] (SEQ ID NO: 104); and

H-Ser-Val-Ser-Glu-Ile-Gln-Leu-Met-His-Asn-Leu-Gly-Lys-His-Leu-Asn-Ser-Met-Glu-Arg-Val-Glu-Trp-Leu-Arg-Lys-Lys-Leu-Gln-Asp-Val-His-Asn-Phe-$(Lys\text{-}Glu)_3$-OH (PTH 1-34 human-$(Lys\text{-}Glu)_3$-OH) [SEQ ID NO.] (SEQ ID NO: 105).

52. (Amended) A peptide conjugate comprising X and Z,

wherein X is a pharmacologically active heteropolymeric peptide sequence, and

wherein Z is a stabilising peptide sequence of 4-20 amino acid units covalently bound by its N terminus to the C terminus end of X, wherein each amino acid unit in said stabilising peptide sequence Z is [selected from the group consisting of] Ala, Leu, Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His, Met, Orn, [and] or amino acid units of the general formula I

$$-NH-C(R^1)(R^2)-C(=O)- \qquad (I)$$

wherein R^1 and R^2 are selected from the group consisting of hydrogen, C_{1-6}-alkyl, phenyl, and phenyl-methyl, wherein C_{1-6}-alkyl is optionally substituted with from one to three substituents

selected from halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, and phenyl and phenyl-methyl is optionally substituted with from one to three substituents selected from C_{1-6}-alkyl, C_{2-6}-alkenyl, halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, or R^1 and R^2 together with the carbon atom to which they are bound form a cyclopentyl, cyclohexyl, or cycloheptyl ring; and

wherein the ratio between the half-life of said peptide conjugate and the half-life of the corresponding pharmacologically active peptide sequence X, when treated with carboxypeptidase A or leucine aminopeptidase in about 50 mM phosphate buffer solution at about pH 7.4 at about 37°C or in serum or plasma is at least 3; or a salt thereof[, wherein Z comprises at least two identical amino acid units].

55. (Amended) The peptide conjugate of claim 1 [54], wherein Z consists of about 4 to about 7 amino acid units.

58. (Amended) The peptide conjugate of claim 1 [57], wherein Z comprises at least [four or] five Lys amino acid units.

64. (Amended) A peptide conjugate comprising X and Z,

wherein X is a pharmacologically active heteropolymeric peptide sequence, and

wherein Z is a stabilising peptide sequence of 4-20 amino acid units covalently bound by its N terminus to the C terminus end of X, wherein each amino acid unit in said stabilising peptide sequence Z is [selected from the group consisting of] Ala, Leu, Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His, Met, Orn, [and] or amino acid units of the general formula I

$$-NH-C(R^1)(R^2)-C(=O)- \qquad (I)$$

wherein R^1 and R^2 are selected from the group consisting of hydrogen, C_{1-6}-alkyl, phenyl, and phenyl-methyl, wherein C_{1-6}-alkyl is optionally substituted with from one to three substituents selected from halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, and phenyl and phenyl-methyl is optionally substituted with from one to three substituents selected from C_{1-6}-alkyl, C_{2-6}-alkenyl, halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, or R^1 and R^2 together with the carbon atom to which they are bound form a cyclopentyl, cyclohexyl, or cycloheptyl ring; and

wherein the ratio between the half-life of said peptide conjugate and the half-life of the corresponding pharmacologically active peptide sequence X, when treated with carboxypeptidase A or leucine aminopeptidase in about 50 mM phosphate buffer solution at about pH 7.4 at about 37°C or in serum or plasma is at least 2; or a salt thereof, wherein said pharmacologically active peptide sequence (X) consists of at the most about 65 amino acid units [, wherein Z comprises at least two identical amino acid units].

68. (Amended) A peptide conjugate comprising X and Z,

wherein X is a pharmacologically active heteropolymeric peptide sequence, and

wherein Z is a stabilising peptide sequence of 4-20 amino acid units covalently bound by its N terminus to the C terminus end of X, wherein [each amino acid unit in said stabilising peptide sequence] Z is $\underline{Lys_p\text{-}Xaa_q}$ or $\underline{Xaa_p\text{-}Lys_q}$, wherein p and q are integers in the range from 1 to 14, with the proviso that p+q is in the range of 4-15, and each Xaa is Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Arg, His, Orn, 2,4-diaminobutanoic acid, 2,3-diaminopropanoic acid or Met [selected from the group consisting of Ala, Leu, Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His, Met, Orn, and amino acid units of the general formula I

$$-NH\text{-}C(R^1)(R^2)\text{-}C(=O)- \qquad (I)$$

wherein R^1 and R^2 are selected from the group consisting of hydrogen, C_{1-6}-alkyl, phenyl, and phenyl-methyl, wherein C_{1-6}-alkyl is optionally substituted with from one to three substituents selected from halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, and phenyl and phenyl-methyl is optionally substituted with from one to three substituents selected from C_{1-6}-alkyl, C_{2-6}-alkenyl, halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, or R^1 and R^2 together with the carbon atom to which they are bound form a cyclopentyl, cyclohexyl, or cycloheptyl ring]; and

wherein the ratio between the half-life of said peptide conjugate and the half-life of the corresponding pharmacologically active peptide sequence X, when treated with carboxypeptidase A or leucine aminopeptidase in about 50 mM phosphate buffer solution at about pH 7.4 at about 37°C or in serum or plasma is at least 2; or a salt thereof,

wherein,

[Z is Lys_p-Xaa_q or Xaa_p-Lys_q, wherein p and q are integers in the range from 1 to 14, with the proviso that p+q is in the range of 3-15, and each Xaa is independently selected from the group consisting of Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Arg, His, Orn, 2,4-diaminobutanoic acid, 2,3-diaminopropanoic acid and Met,

and further wherein,]

X is selected from the group consisting of AF 12505 (Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala) (SEQ ID [NO.] NO: 14), insulin-like growth factor I (57-70) (Ala-Leu-Leu-Glu-Thr-Tyr-Cys-Ala-Thr-Pro-Ala-Lys-Ser-Glu) [SEQ ID NO.] (SEQ ID NO: 15), insulin-like growth factor I (30-41) (Gly-Tyr-Gly-Ser-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr) [SEQ ID NO.] (SEQ ID NO: 16), insulin-like growth factor I (24-41)(Tyr-Phe-Asn-Lys-Pro-Thr-Gly-Tyr-Gly-Ser-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr) [SEQ ID NO.] (SEQ ID NO: 17) , insulin-like growth factor II (33-40) (Ser-Arg-Val-Ser-Arg-Arg-Ser-Arg) [SEQ ID NO.] (SEQ ID NO: 18), insulin-like growth factor II (33-40) (Tyr-Ser-Arg-Val-Ser-Arg-Arg-Ser-Arg) [SEQ ID NO.] (SEQ ID NO: 19), insulin-like growth factor II (69-84) (Asp-Val-Ser-Thr-Pro-Pro-Thr-Val-Leu-Pro-Asp-Asn-Phe-Pro- Arg-Tyr) [SEQ ID NO.] (SEQ ID NO: 20), growth hormone (GH)-releasing peptide-6 (GHRP-6) (His-DTrp-Ala-Trp-DPhe-Lys-NH2) [SEQ ID NO.] (SEQ ID NO: 21), beta-Interleukin I (163-171) (Val-Gln-Gly-Glu-Glu-Ser-Asn-Asp-Lys) [SEQ ID NO.] (SEQ ID

NO: 22), beta-Interleukin II (44-56) (Ile-Leu-Asn-Gly-Ile-Asn-Asn-Tyr-Lys-Asn-Pro-Lys-Leu) [SEQ ID NO.] (SEQ ID NO: 23), Interleukin II (60-70) (Leu-Thr-Phe-Lys-Phe-Tyr-Met-Pro-Lys-Lys-Ala) [SEQ ID NO.] (SEQ ID NO: 24), exendin-4 (GLP-1 analog) (His-Gly-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH2) [SEQ ID NO.] (SEQ ID NO: 25), exendin-3 (GLP-1 analog) (His-Ser-Asp-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser) [SEQ ID NO.] (SEQ ID NO: 26), epidermal growth factor (20-31) Cys(Acm)-Met-His-Ile-Glu-Ser-Leu-Asp-Ser-Tyr-Thr-Cys(Acm) [SEQ ID NO.] (SEQ ID NO: 27), bivalirudin (Hirulog) (D-Phe-Pro-Arg-Pro-(Gly)4-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Glu-Tyr-Leu) [SEQ ID NO.] (SEQ ID NO: 28), hirulog-1 D-Phe-Pro-Arg-Pro-(Gly)4-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Tyr-Leu [SEQ ID NO.] (SEQ ID NO: 29), C-type natriuretic peptide (1-53) (CNP) (Asp-Leu-Arg-Val-Asp-Thr-Lys-Ser-Arg-Ala-Ala-Trp-Ala-Arg-Leu-Leu-Gln-Glu-His-Pro-Asn-Ala-Arg-Lys-Tyr-Lys-Gly-Ala-Asn-Lys-Lys-Gly-Leu-Ser-Lys-Gly-Cys-Phe-Gly-Leu-Lys-Leu-Asp-Arg-Ile-Gly-Ser-Met-Ser-Gly-Leu-Gly-Cys; Disulfide bridge: Cys37-Cys53) [SEQ ID NO.] (SEQ ID NO: 30), "Mini ANP" (Met-Cys-His-cyclohexylAla-Gly-Gly-Arg-Met-Asp-Arg-Ile-Ser-Cys-Tyr-Arg, disulfide bridge cys2-cys13) [SEQ ID NO.] (SEQ ID NO: 31), Melanotan-II (MT-II, alpha-MSH4-10-NH2, or Ac-Nle4-Asp5-His6-D-Phe7-Arg8-Trp9-Lys10) [SEQ ID NO.] (SEQ ID NO: 32), thymosin alpha1 (TA1) (Ac-Ser-Asp-Ala-Ala-Val-Asp-Thr-Ser-Ser-Glu-Ile-Thr-Thr-Lys-Asp-Leu-Lys-Glu-Lys-Lys-Glu-Val-Val-Glu-Glu-Ala-Glu-Asn) [SEQ ID NO.] (SEQ ID NO: 33), Cys-Phe-Ile-Gln-Asn-Cys-Pro-Orn-Gly-NH2, Disulfide bridge: Cys1-Cys6) [SEQ ID NO.] (SEQ ID NO: 34), octreotide (201-995) (DPhe-Cys-Phe-DTrp-Lys-Thr-Cys-Thr-ol; disulfide bridge: Cys2-Cys7) [SEQ ID NO.] (SEQ ID NO: 35), calcitonin gene-related peptide (CGRP) (Ala-Cys-Asp-Thr-Ala-Thr-Cys-Val-Thr-His-Arg-Leu-Ala-Gly-Leu-Leu-Ser-Arg-Ser-Gly-Gly-Val-Val-Lys-Asn-Asn-Phe-Val-Pro-Thr-Asn-Val-Gly-Ser-Lys-Ala-Phe-NH_2; Disulfide bridge: Cys2-Cys7) [SEQ ID NO.] (SEQ ID NO: 36), endomorphin-1 Tyr-Pro-Trp-Phe-NH2 [SEQ ID NO.] (SEQ ID NO: 37); endomorphin-2 Tyr-Pro-Phe-Phe-NH_2 [SEQ ID NO.] (SEQ ID NO: 38), nociceptin (also known as Orphanin FQ, Phe-Gly-Gly-Phe-Thr-Gly-Ala-Arg-Lys-Ser-Ala-Arg-Lys-Leu-Ala-Asn-Gln) [SEQ ID NO.] (SEQ ID NO: 39), angiotensinogen (1-13) (Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-

His) [SEQ ID NO.] (SEQ ID NO: 40), adrenomodullin (1-12) (Tyr-Arg-Gln-Ser-Met-Asn-Asn-Phe-Gln-Gly-Leu-Arg) [SEQ ID NO.] (SEQ ID NO: 41), antiarrhytmic peptide (AAP) (Gly-Pro-Hyp-Gly-Ala-Gly) [SEQ ID NO.] (SEQ ID NO: 42), Antagonist G (Arg-DTrp-(nMe)Phe-DTrp-Leu-Met-NH_2), indolicidin (Ile-Leu-Pro-Trp-Lys-Trp-Pro-Trp-Trp-Pro-Trp-Arg-Arg-NH_2) [SEQ ID NO.] (SEQ ID NO: 43), osteocalcin (37-49) (Gly-Phe-Gln-Glu-Ala-Tyr-Arg-Arg-Phe-Tyr-Gly-Pro-Val) [SEQ ID NO.] (SEQ ID NO: 44), cortistatin 29 (1-13) (Glp)-Glu-Arg-Pro-Pro-Leu-Gln-Gln-Pro-Pro-His-Arg-Asp) [SEQ ID NO.] (SEQ ID NO: 45), cortistatin 14 Pro-Cys-Lys-Asn-Phe-Phe-Trp-Lys-Thr-Phe-Ser-Ser-Cys-Lys; Disulfide bridge: Cys2-Cys13 [SEQ ID NO.] (SEQ ID NO: 46), PD-145065 (Ac-D-Bhg-Leu-Asp-Ile-Ile-Trp) [SEQ ID NO.] (SEQ ID NO: 47), PD-142893 (Ac-D-Dip-Leu-Asp-Ile-Ile-Trp) [SEQ ID NO.] (SEQ ID NO: 48), fibrinogen binding inhibitor peptide (His-His-Leu-Gly-Gly-Ala-Lys-Gln-Ala-Gly-Asp-Val) [SEQ ID NO.] (SEQ ID NO: 49), leptin (93-105) (Asn-Val-Ile-Gln-Ile-Ser-Asn-Asp-Leu-Glu-Asn-Leu-Arg) [SEQ ID NO.] (SEQ ID NO: 50), GR 83074 (Boc-Arg-Ala-DTrp-Phe-DPro-Pro-Nle-NH_2) [SEQ ID NO.] (SEQ ID NO: 51) Tyr-W-MIF-1 (Tyr-Pro-Trp-Gly-NH_2) [SEQ ID NO.] (SEQ ID NO: 52), parathyroid hormone related peptide (107-111) (Thr-Arg-Ser-Ala-Trp) [SEQ ID NO.] (SEQ ID NO: 53), angiotensinogen (1-14) Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His-Asn [SEQ ID NO.] (SEQ ID NO: 54), and Leupeptin (Ac-Leu-Leu-Arg-CHO) [;further wherein Z comprises at least two identical amino acid units].

75. (Amended) A composition comprising a pharmaceutically acceptable carrier, and a conjugate according to claim 1 in an amount effective to stimulate [erythroposiesis] erythropoiesis.

77. (Amended) The peptide conjugate of claim 1, wherein the conjugate is represented by the following sequence: Ac-Ser-Tyr-Ser-Met-Glu-His-Phe-Arg-Trp-Gly-Lys-Pro-Val-$(Lys)_6$-NH_2 (SEQ ID NO: 122) or a fragment thereof.

The following new claims 78-81 have been added:

78. (New) A peptide conjugate consisting of X and Z,

wherein X is a pharmacologically active heteropolymeric peptide sequence, and

wherein Z is a stabilising peptide sequence of 4-20 amino acid units covalently bonded by its N terminus to the C terminus end of X wherein each amino acid unit in said stabilising peptide sequence Z is Ala, Leu, Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His, Met, Orn, or amino acid units of the general formula I

$$-NH-C(R^1)(R^2)-C(=O)- \qquad (I)$$

wherein R^1 and R^2 are selected from the group consisting of hydrogen, C_{1-6}-alkyl, phenyl, and phenyl-methyl, wherein C_{1-6}-alkyl is optionally substituted with from one to three substituents selected from halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, and phenyl and phenyl-methyl is optionally substituted with from one to three substituents selected from C_{1-6}-alkyl, C_{2-6}-alkenyl, halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, or R^1 and R^2 together with the carbon atom to which they are bound form a cyclopentyl, cyclohexyl, or cycloheptyl ring; and

wherein the ratio between the half-life of said peptide conjugate and the half-life of the corresponding pharmacologically active peptide sequence, X, when treated with carboxypeptidase A or leucine aminopeptidase in about 50 mM phosphate buffer solution at about pH 7.4 at about 37°C or in serum or plasma is at least 2; or a salt thereof.

79. (New) A peptide conjugate consisting of X and Z,

wherein X is a pharmacologically active heteropolymeric peptide sequence, and

wherein Z is a stabilising peptide sequence of 4-20 amino acid units covalently bound by its N terminus to the C terminus end of X, wherein each amino acid unit in said stabilising peptide sequence Z is Ala, Leu, Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His, Met, Orn, or amino acid units of the general formula I

$$-NH-C(R^1)(R^2)-C(=O)- \qquad (I)$$

wherein R^1 and R^2 are selected from the group consisting of hydrogen, C_{1-6}-alkyl, phenyl, and phenyl-methyl, wherein C_{1-6}-alkyl is optionally substituted with from one to three substituents selected from halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, and phenyl and phenyl-methyl is optionally substituted with from one to three substituents selected from C_{1-6}-alkyl, C_{2-6}-alkenyl, halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, or R^1 and R^2 together with the carbon atom to which they are bound form a cyclopentyl, cyclohexyl, or cycloheptyl ring; and

wherein the ratio between the half-life of said peptide conjugate and the half-life of the corresponding pharmacologically active peptide sequence X, when treated with carboxypeptidase A or leucine aminopeptidase in about 50 mM phosphate buffer solution at about pH 7.4 at about 37°C or in serum or plasma is at least 3; or a salt thereof.

80. (New) A peptide conjugate consisting of X and Z,

wherein X is a pharmacologically active heteropolymeric peptide sequence, and

wherein Z is a stabilising peptide sequence of 4-20 amino acid units covalently bound by its N terminus to the C terminus end of X, wherein each amino acid unit in said stabilising peptide sequence Z is Ala, Leu, Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Lys, Arg, His, Met, Orn, or amino acid units of the general formula I

$$-NH-C(R^1)(R^2)-C(=O)- \qquad (I)$$

wherein R^1 and R^2 are selected from the group consisting of hydrogen, C_{1-6}-alkyl, phenyl, and phenyl-methyl, wherein C_{1-6}-alkyl is optionally substituted with from one to three substituents selected from halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, and phenyl and

phenyl-methyl is optionally substituted with from one to three substituents selected from C_{1-6}-alkyl, C_{2-6}-alkenyl, halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, or R^1 and R^2 together with the carbon atom to which they are bound form a cyclopentyl, cyclohexyl, or cycloheptyl ring; and

wherein the ratio between the half-life of said peptide conjugate and the half-life of the corresponding pharmacologically active peptide sequence X, when treated with carboxypeptidase A or leucine aminopeptidase in about 50 mM phosphate buffer solution at about pH 7.4 at about 37°C or in serum or plasma is at least 2; or a salt thereof, wherein said pharmacologically active peptide sequence (X) consists of at the most about 65 amino acid units.

81. (New) A peptide conjugate consisting of X and Z,

wherein X is a pharmacologically active heteropolymeric peptide sequence, and

wherein Z is a stabilising peptide sequence of 4-20 amino acid units covalently bound by its N terminus to the C terminus end of X, wherein Z is Lys_p-Xaa_q or Xaa_p-Lys_q, wherein p and q are integers in the range from 1 to 14, with the proviso that p+q is in the range of 4-15, and each Xaa is Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Arg, His, Orn, 2,4-diaminobutanoic acid, 2,3-diaminopropanoic acid or Met; and

wherein the ratio between the half-life of said peptide conjugate and the half-life of the corresponding pharmacologically active peptide sequence X, when treated with carboxypeptidase A or leucine aminopeptidase in about 50 mM phosphate buffer solution at about pH 7.4 at about 37°C or in serum or plasma is at least 2; or a salt thereof,

wherein,

X is selected from the group consisting of AF 12505 (Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala) (SEQ ID NO: 14), insulin-like growth factor I (57-70) (Ala-Leu-Leu-Glu-Thr-Tyr-Cys-Ala-Thr-Pro-Ala-Lys-Ser-Glu) (SEQ ID NO: 15), insulin-like growth factor I (30-41) (Gly-Tyr-Gly-Ser-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr) (SEQ ID NO: 16), insulin-

like growth factor I (24-41)(Tyr-Phe-Asn-Lys-Pro-Thr-Gly-Tyr-Gly-Ser-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr) (SEQ ID NO: 17) , insulin-like growth factor II (33-40) (Ser-Arg-Val-Ser-Arg-Arg-Ser-Arg) (SEQ ID NO: 18), insulin-like growth factor II (33-40) (Tyr-Ser-Arg-Val-Ser-Arg-Arg-Ser-Arg) (SEQ ID NO: 19), insulin-like growth factor II (69-84) (Asp-Val-Ser-Thr-Pro-Pro-Thr-Val-Leu-Pro-Asp-Asn-Phe-Pro- Arg-Tyr) (SEQ ID NO: 20), growth hormone (GH)-releasing peptide-6 (GHRP-6) (His-DTrp-Ala-Trp-DPhe-Lys-NH2) (SEQ ID NO: 21), beta-Interleukin I (163-171) (Val-Gln-Gly-Glu-Glu-Ser-Asn-Asp-Lys) (SEQ ID NO: 22), beta-Interleukin II (44-56) (Ile-Leu-Asn-Gly-Ile-Asn-Asn-Tyr-Lys-Asn-Pro-Lys-Leu) (SEQ ID NO: 23), Interleukin II (60-70) (Leu-Thr-Phe-Lys-Phe-Tyr-Met-Pro-Lys-Lys-Ala) (SEQ ID NO: 24), exendin-4 (GLP-1 analog) (His-Gly-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH2) (SEQ ID NO: 25), exendin-3 (GLP-1 analog) (His-Ser-Asp-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser) (SEQ ID NO: 26), epidermal growth factor (20-31) Cys(Acm)-Met-His-Ile-Glu-Ser-Leu-Asp-Ser-Tyr-Thr-Cys(Acm) (SEQ ID NO: 27), bivalirudin (Hirulog) (D-Phe-Pro-Arg-Pro-(Gly)4-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Glu-Tyr-Leu) (SEQ ID NO: 28), hirulog-1 D-Phe-Pro-Arg-Pro-(Gly)4-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Tyr-Leu (SEQ ID NO: 29), C-type natriuretic peptide (1-53) (CNP) (Asp-Leu-Arg-Val-Asp-Thr-Lys-Ser-Arg-Ala-Ala-Trp-Ala-Arg-Leu-Leu-Gln-Glu-His-Pro-Asn-Ala-Arg-Lys-Tyr-Lys-Gly-Ala-Asn-Lys-Lys-Gly-Leu-Ser-Lys-Gly-Cys-Phe-Gly-Leu-Lys-Leu-Asp-Arg-Ile-Gly-Ser-Met-Ser-Gly-Leu-Gly-Cys; Disulfide bridge: Cys37-Cys53) (SEQ ID NO: 30), "Mini ANP" (Met-Cys-His-cyclohexylAla-Gly-Gly-Arg-Met-Asp-Arg-Ile-Ser-Cys-Tyr-Arg, disulfide bridge cys2-cys13) (SEQ ID NO: 31), Melanotan-II (MT-II, alpha-MSH4-10-NH2, or Ac-Nle4-Asp5-His6-D-Phe7-Arg8-Trp9-Lys10) (SEQ ID NO: 32), thymosin alpha1 (TA1) (Ac-Ser-Asp-Ala-Ala-Val-Asp-Thr-Ser-Ser-Glu-Ile-Thr-Thr-Lys-Asp-Leu-Lys-Glu-Lys-Lys-Glu-Val-Val-Glu-Glu-Ala-Glu-Asn) (SEQ ID NO: 33), Cys-Phe-Ile-Gln-Asn-Cys-Pro-Orn-Gly-NH2, Disulfide bridge: Cys1-Cys6) (SEQ ID NO: 34), octreotide (201-995) (DPhe-Cys-Phe-DTrp-Lys-Thr-Cys-Thr-ol; disulfide bridge: Cys2-Cys7) (SEQ ID NO: 35), calcitonin gene-related peptide (CGRP) (Ala-Cys-Asp-Thr-Ala-Thr-Cys-Val-Thr-His-Arg-Leu-Ala-Gly-Leu-Leu-Ser-Arg-Ser-Gly-Gly-Val-Val-Lys-Asn-Asn-Phe-Val-Pro-Thr-Asn-Val-Gly-Ser-Lys-Ala-Phe-NH_2;

Disulfide bridge: Cys2-Cys7) (SEQ ID NO: 36), endomorphin-1 Tyr-Pro-Trp-Phe-NH2 (SEQ ID NO: 37); endomorphin-2 Tyr-Pro-Phe-Phe-NH_2 (SEQ ID NO: 38), nociceptin (also known as Orphanin FQ, Phe-Gly-Gly-Phe-Thr-Gly-Ala-Arg-Lys-Ser-Ala-Arg-Lys-Leu-Ala-Asn-Gln) (SEQ ID NO: 39), angiotensinogen (1-13) (Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His) (SEQ ID NO: 40), adrenomodullin (1-12) (Tyr-Arg-Gln-Ser-Met-Asn-Asn-Phe-Gln-Gly-Leu-Arg) (SEQ ID NO: 41), antiarrhytmic peptide (AAP) (Gly-Pro-Hyp-Gly-Ala-Gly) (SEQ ID NO: 42), Antagonist G (Arg-DTrp-(nMe)Phe-DTrp-Leu-Met-NH_2), indolicidin (Ile-Leu-Pro-Trp-Lys-Trp-Pro-Trp-Trp-Pro-Trp-Arg-Arg-NH_2) (SEQ ID NO: 43), osteocalcin (37-49) (Gly-Phe-Gln-Glu-Ala-Tyr-Arg-Arg-Phe-Tyr-Gly-Pro-Val) (SEQ ID NO: 44), cortistatin 29 (1-13) (Glp)-Glu-Arg-Pro-Pro-Leu-Gln-Gln-Pro-Pro-His-Arg-Asp) (SEQ ID NO: 45), cortistatin 14 Pro-Cys-Lys-Asn-Phe-Phe-Trp-Lys-Thr-Phe-Ser-Ser-Cys-Lys; Disulfide bridge: Cys2-Cys13 (SEQ ID NO: 46), PD-145065 (Ac-D-Bhg-Leu-Asp-Ile-Ile-Trp) (SEQ ID NO: 47), PD-142893 (Ac-D-Dip-Leu-Asp-Ile-Ile-Trp) (SEQ ID NO: 48), fibrinogen binding inhibitor peptide (His-His-Leu-Gly-Gly-Ala-Lys-Gln-Ala-Gly-Asp-Val) (SEQ ID NO: 49), leptin (93-105) (Asn-Val-Ile-Gln-Ile-Ser-Asn-Asp-Leu-Glu-Asn-Leu-Arg) (SEQ ID NO: 50), GR 83074 (Boc-Arg-Ala-DTrp-Phe-DPro-Pro-Nle-NH_2) (SEQ ID NO: 51) Tyr-W-MIF-1 (Tyr-Pro-Trp-Gly-NH_2) (SEQ ID NO: 52), parathyroid hormone related peptide (107-111) (Thr-Arg-Ser-Ala-Trp) (SEQ ID NO: 53), angiotensinogen (1-14) Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His-Asn (SEQ ID NO: 54), and Leupeptin (Ac-Leu-Leu-Arg-CHO).